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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,663	09/23/2003	Victor C. Yang	4100.001482	5598

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/668,663	YANG ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-50 and 55-70* is/are pending in the application.

4a) Of the above claim(s) *57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-50,55,56 and 59-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed October 12, 2005 on April 18, 2006 is acknowledged.

Claim Disposition

2. Claims 1-47 and 51-54 have been cancelled. Claims 69-70 have been added. Claims 48-50 and 55-70 are pending. Claims 40-50, 55-56 and 59-70 are under examination.

Information Disclosure Statement

3. As previously stated the information disclosure statement filed on January 26, 2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP 609 because items listed on the information disclosure statement are missing from the application. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. It is noted that applicant state that copies of the references were provided, however, none have been found. It is suggested that Applicant resubmit the references for consideration. A line has been drawn through all references listed on the PTO-1449 form that are non-patent literature, all others have been considered.

Maintained-Specification Objection

4. The specification is objected to because of the following informalities:

The specification is objected to because trademarks are disclosed throughout the instant specification and not all of them are capitalized or accompanied by the generic terminology. The use of the trademarks such as TWEEN-20®, TRIS®, for example, have been noted in this application (see page 62). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Correction of the above is required.

Claim Objection

5. The claims are objected to because of the following informalities:

Claims 48-50 and 59-63 are objected to for improper dependency.

Correction is required.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 48-50, 55-56 and 59-70 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a method of inactivating heparin or low molecular weight heparin with purified protamine. The claims are defined only by functional properties, not by a structure. Thus, there is no indication of which purified protamine the claimed invention is directed to. Note for example that claim 67 is directed to a first and second protamine, which provides evidence that there can be more than one protamine, however, no structure is provided. In addition the claims are directed to a method that utilizes the undefined protamine and a second coagulant (see claim 63), which is also undefined. Furthermore, the art teaches that protamine given to neutralize heparin after extracorporeal circulation can trigger a catastrophic reaction in some patients (see Tan et al. Anesthesiology, Feb. 1989, vol. 70, no. 2, pages 267-75). Therefore, the claimed invention needs to adequately describe the protamine intended in the method. Thus the claims lack adequate written description to demonstrate to a skilled artisan that applicant was in possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. See *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997)*. Therefore, a biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written

description purposes, even when accompanied by a method of obtaining the claimed sequence. For example, even though a genetic code table would correlate a known amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native, naturally occurring nucleic acid sequence of a naturally occurring mRNA or its corresponding cDNA. *See MPEP 2163.* The newly submitted claim also lack adequate written description because the claim does not set forth what effect of heparin is intended.

Further, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991),* states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of encoded proteins, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993). See MPEP 2163.*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 48-50, 55-56 and 59-70 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 55 is indefinite for the recitation of "a protamine" as it appears the protamine of the invention is modified such that it differs from the native protamine as the molecular weight is lower; and therefore said protamine may not be a full length structure. Hence the need for clarification in the claim either by structure or definition of how the claimed protamine differs from the native.

Claims 59-62 and 64 lacks clear antecedent basis as the independent claim 55 is directed to a method to inactivate heparin by administering a purified protamine in a composition, thus, the health conditions of the mammal is not a step in the method of inactivation of heparin. The necessary step required is contacting the heparin with the protamine composition as recited in claim 55.

Claim 63 is indefinite for the recitation of "at least a second coagulant" as there is no *per se* reference to a first coagulant.

Claim 69 is indefinite for the recitation of "ameliorates an effect of heparin or low molecular weight heparin" as it is unclear what effect of heparin is resolved.

Claim 70 is indefinite for the recitation of "The method of claim 55(Previously Presented)"

Response to Arguments

8. The response filed on April 18, 2006 has been considered, however, is not fully persuasive. Note that new grounds of rejections have been instituted under 35 U.S.C. 112, second paragraph for the reasons stated above. In addition, the rejections under 35 U.S.C. 112 first and second paragraphs have been maintained. Further, new objections have been made to the claims and the objection to the specification remains as applicant did not amend the specification (see comments on page 5 of the response). Applicant's comments regarding the IDS are noted, however, the references that have been lined through were not found. Applicant is urged to resubmit the references for consideration.

Regarding the rejection under 35 U.S.C. 112, first paragraph, Applicant on page 5+ states that the examiner over looks that protamines are well known in the art. This argument is not persuasive as claim 55 attempts to make a comparison between native protamine and the protamine as claimed. Further, the specification indicates that native protamine is 4500 Daltons thus, it appears that the claimed protamine is modified. The protamine claimed has a molecular weight of 400 to 2500 Daltons, which provides evidence that it differs from the native, maybe a fragment and said structure would not necessarily be in the art. It is noted that applicant on page 7 state that "...given that it was know that full length protamines, i.e. those protamines that which have not been reduced in size by whatever means, neutralize heparin because of a sufficiently polycationic charge, it naturally follows that the LMW protamines for use in the presently claimed methods possess the same polycationic characteristic in order to function in the same way". This statement could be construed as admitted prior art. In addition, applicants indicate that the structure function relationship for protamines was previously known, and what

was not known, was that proteolytically cleaved protamine would have the same property of neutralizing heparin and provide the benefit of reduced toxic effects. The claims do not provide this distinction, hence the reason for the written description rejection. The claims do not set forth how the claimed protamine differs from the native protamine. For example, the claims could recite "a modified protamine" and indicate how said protamine differs from the native. Applicants arguments have been considered in full but are not persuasive for the reasons stated herein and above, thus the rejection remains.

With regard to the rejection under 35 U.S.C. 112, second paragraph, applicant state that the method is being limited by the type of recipient patient even though the steps would otherwise be the same. This argument is not persuasive as independent claim 55 does not require that said method occurs in a mammal or require administration of the composition to a mammal. The claimed method is directed to a method to inactivate heparin/LMW heparin. Therefore applicant's arguments are not persuasive and the rejection remains.

Conclusion

9. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS 6/22/06

Patent Examiner

HOPE ROBINSON
PATENT EXAMINER